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10/591,421	09/01/2006	Nobuhiko Fushimi	Q96479	3051

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EXAMINER	
HENRY, MICHAEL C	
ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
03/22/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/591,421	FUSHIMI ET AL.	
	Examiner	Art Unit	
	MICHAEL C. HENRY	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22,27-31 and 35* is/are pending in the application.

4a) Of the above claim(s) *19-22 and 29-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,27,28 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/01/06 & 06/05/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The following office action is a responsive to the Amendment filed, 12/23/09.

Applicant's election without traverse of Group I in the reply filed on 12/23/09 is acknowledged.

Claims 19-22, 29-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/23/09.

The amendment filed 12/23/09 affects the application 10/591,421 as follows:

1. Claims 1-18, 27-28 and 35, the invention of Group I is prosecuted by the examiner. Claims are 19-22, 29-31 are withdrawn.
2. The responsive is contained herein below.

Claims 1-22, 27-31 and 35 are pending in application

Information Disclosure Statement

The information disclosure statement filed complies with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Claim Objections

Claims 17 and 18 are objected to because of the following informalities: The claims recite the phrase "is sustained release formulation" which appears to contain a typographical error. It appears that the phrase should be "is a sustained release formulation". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18, 27-28 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to a fused heterocyclic derivative represented by a general formula (I). However, the claim is indefinite since the symbols or letters A^1 and A^2 in the said general formula (I) are not defined in the claim. Consequently, the identity and the metes and bounds of said derivative that applicant regard as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims.

Claims 14 and 15 recite the phrase "a disease associated with hyperglycemia". However, the claims are indefinite since it is unclear what constitutes or does not constitute an association as recited in the claims.

Claim 17 recites the phrase "A pharmaceutical composition as claimed in claim 10, wherein the dosage form is sustained release formulation". However, the claim is indefinite since it is unclear whether a dosage form is claimed or a pharmaceutical composition in a dosage form. Furthermore, it is unclear how the dosage form differs from the pharmaceutical composition that is not in a dosage especially since the characteristics of said dosage form with respect to amounts, quantities are unknown. Also, it unclear what method or process involves a

sustained release of said composition and if said composition must be tested in said process in order to practice applicant's invention.

Claim 18 recites the phrase "A human SGLT inhibitor as claimed in claim 11, wherein the dosage form is sustained release formulation". However, the claim is indefinite since it is unclear whether a dosage form is claimed or a human SGLT inhibitor in a dosage form. Furthermore, it is unclear how the dosage form differs from the human SGLT inhibitor (composition) that is not in a dosage especially since the characteristics of said dosage form with respect to amounts or quantities are unknown. Also, it unclear what method or process involves a sustained release of said composition and if said composition must be tested in said process in order to practice applicant's invention.

The term "carnitine derivative" in claim 27 and 28 renders the claims indefinite. More specifically, in the absence of the specific derivatizations to the chemical core claimed (CCC) or distinct language to describe the structural modifications or the chemical names of the derivatized (CCC) of this invention, the identity of said derivatives would be difficult to describe and the metes and bounds of said derivatives that applicant regard as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims. Therefore, the identity of this composition component is indefinite. Similarly, the term "nicotinic acid derivative" is seen to be indefinite since applicant fails to provide how the core compound is modified to obtain some derivatized version which is intended to be an integral part of the composition claimed.

Similarly, the term "a glucagon-like peptide-1 analogue" in claim 27 and 28 renders the claims indefinite. More specifically, in the absence of distinct language to describe the structural

modifications or the chemical names of the analogue of this invention, the identity of said analogue would be difficult to describe and the metes and bounds of said analogue that applicant regard as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims. Therefore, the identity of this composition component is indefinite. Similarly, the terms "an amylin analogue" and "a platelet-derived growth factor analogue"are seen to be indefinite since applicant fails to provide how the core compound is modified to obtain some analogue version which is intended to be an integral part of the composition claimed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition or agent for treating specific diseases such as obesity or diabetes in a patient, does not reasonably provide enablement for preventing said diseases including obesity or diabetes in a patient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would

have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The nature of the invention: The instant invention pertains to a human SGLT inhibitor which is an agent for the prevention or treatment of a disease associated with hyperglycemia.

The relative skill of those in the art: The relative skill of those in the art is high. The examiner notes that the knowledge and level of skill in this art would not permit one skilled in this art to assert a preventive therapeutic mode of administration and the skilled artisan could not immediately envisage the invention claimed.

The breadth of the claims: The instant claims are deemed very broad since these claims reads on a composition for preventing or treating several diseases including obesity or diabetes (in any and all kinds of subjects).

Regarding the *Wands* factor (4) the predictability or unpredictability of the art:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that the recitation encompasses a composition for preventing and treating numerous diseases including obesity

or diabetes (in any and all kinds of subjects), which are not known to have a single recognized cause. Applicant claims a composition for preventing and treating numerous diseases including obesity or diabetes, which is not generally known to exist in this art; additionally, the disclosure is silent with regard to that which makes up and identifies the method for preventing the said diseases including obesity or diabetes with the claimed composition, which is seen to be lacking a clear description via art recognized procedural and methodological steps. Furthermore, the prevention of said diseases such as obesity or diabetes which are characterized as being numerous unpredictable ones, do not have a single recognized cause. In fact, the aforementioned obesity or diabetes, are recognized as having many contributing factors, ranging from hereditary considerations, to lifestyles choices such as the diet and maintenance of bodily healthiness which can be complicated by existing physical or medical conditions in the patient such as (1) high blood glucose (blood sugar) levels (2) high blood pressure (2) high cholesterol (3) family history of heart disease, stroke or diabetes (4) physical inactivity (5) age (6) weight.

These are only a few of the factors that promote these diseases or conditions in patients or people. Applicant has not provided a description as how any cause (like the aforementioned) can be prevented, much less a description of how the said conditions can be prevented.

Thus, the skilled artisan would view that the prevention of the said diseases including obesity or diabetes (which is characterized as having many contributing factors and causes) in a patient by administering to said patient the specific composition, compound or inhibitor herein, as being highly *unpredictable*.

In regard to these *Wands* factors, (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary: Moreover, it is noted that the specification provides no working examples to the prevention of said diseases including obesity or diabetes.

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the prevention of obesity or diabetes as recited in the instant claims. As a result, necessitating one of skill to perform an exhaustive search for the embodiments of preventing said diseases such as obesity or diabetes in any subject or patient for the composition as recited in the instant claims suitable to practice the claimed invention. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict the efficacy of the claimed method with a reasonable expectation of success. Therefore, a composition for the prevention of said diseases including obesity or diabetes is not enabled by the instant disclosure.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation*, with no assurance of success.

Claims 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for a pharmaceutical composition as claimed in claim 10, which comprises a combination with specific substances or compounds such as acarbose and voglibose, it does not reasonably provide enablement for a pharmaceutical composition as claimed in claim 10, which comprises a combination with all or any of the numerous classes or groups of substances or compounds recited in claim 27.

For example, all or any one of the numerous classes or groups of substances or compounds, would reasonably broadly encompass those known and unknown compounds as of the instant filing date.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

1. The nature of the invention: The instant invention pertains to a pharmaceutical composition comprising as an active ingredient a fused heterocyclic derivative, or a pharmaceutically acceptable salt thereof, or a prodrug thereof, which comprises combination with at least one member selected from the group consisting of numerous classes or groups of

substances or compounds including an insulin sensitivity enhancer, a glucose absorption inhibitor, a biguanide, an insulin secretion enhancer, a SGLT2 inhibitor, an insulin or insulin analogue, a glucagon receptor antagonist, an insulin receptor kinase stimulant, a tripeptidyl peptidase II inhibitor, a dipeptidyl peptidase IV inhibitor, a protein tyrosine phosphatase-lB inhibitor, a glycogen phosphorylase inhibitor, a glucose-6- phosphatase inhibitor, a fructose-bisphosphatase inhibitor, a pyruvate dehydrogenase inhibitor, a hepatic gluconeogenesis inhibitor, D-chiroinsitol, a glycogen synthase kinase-3 inhibitor, glucagon-like peptide-1, a glucagon-like peptide-1 analogue, a glucagon-like peptide-1 agonist, amylin, an amylin analogue, an amylin agonist, an aldose reductase inhibitor, an advanced glycation endproducts formation inhibitor, a protein kinase C inhibitor, a y-aminobutyric acid receptor antagonist, a sodium channel antagonist, a transcript factor NF-vJ3 inhibitor, which encompasses the numerous compounds known to exist (see claim 27).

2. The state of the prior art: The skilled artisan would view the preparation of pharmaceutical composition comprising the said fused heterocyclic derivative with all the numerous classes or groups of substances or compounds, as not possible.

3. The predictability of the art, and the breadth of the claims:

It is highly unpredictable which compounds or whether or not a particular compound of the numerous groups or classes of compounds can be prepared as a combination with said fused heterocyclic derivative, as required by the claim. Such determination would require numerous or several trails and experimental processes. Also, the preparation or synthesis of novel chemical compounds is highly complex and unpredictable. That is, there is no routine, predictable way to prepare or synthesize each and every novel chemical compound. Rather, specific compounds or

groups of related compounds require individually designed synthetic schemes which must be developed by a process of unpredictable experimentation. In addition, and as example, the claim encompasses a pharmaceutical composition that comprises a combination of the fused heterocyclic derivative together with all the numerous recited members of the group (since all the members can simultaneously be present together with the fused heterocyclic derivative (e.g., see claim 27 or 28) Moreover, it should be noted that the claim encompasses a pharmaceutical composition comprising numerous the said fused heterocyclic derivative with numerous classes or groups of compounds with numerous distinct or unique structures, chemical and physical properties are known to exist in nature.

4. The presence or absence of working examples: It is noted that the specification does not provide a working example of a pharmaceutical composition comprising as an active ingredient a fused heterocyclic derivative, or a pharmaceutically acceptable salt thereof, or a prodrug thereof, which comprises combination the numerous classes or groups of substances or compound. That is, the evidence provided is not commensurate in scope with the claimed invention and does not demonstrate criticality of the numerous compounds that are encompassed by applicant's claimed method. See MPEP § 716.02(d).

Further, those unknown or future known compounds must require additional or future research to discover, synthesize or prepare. Therefore, the skilled artisan has to exercise undue experimentation to practice the instant invention.

Thus, the specification fails to provide sufficient support of the broad number and variety of the compounds or composition that are encompassed by the instant claim. As a result, necessitating one of skill to perform an exhaustive search for the embodiments and

preparation of compounds and compositions that are encompassed by the instant claims that are suitable to practice the claimed invention.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factor and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to prepare compounds encompassed in the instant claims, with no assurance of success.

Similarly, claim 28 which is drawn to a human SGLT inhibitor as claimed in claim 11, which comprises a combination said fused heterocyclic derivative, or a pharmaceutically acceptable salt thereof, or a prodrug thereof, with all or any of the numerous classes or groups of substances or compounds that are recited in said claim are also encompassed by this rejection.

Claims 1-18, 27-28 and 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a fused heterocyclic derivative represented by the following general formula (I) or pharmaceutically acceptable salt thereof, or a specific prodrug of general formula (I) denoted by structure, does not reasonably provide enablement for any prodrug of the general formula (I). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

The Nature of the Invention

The instant invention is drawn to a compound or fused heterocyclic derivative of general formula (I), or pharmaceutically acceptable salts thereof or prodrugs thereof and also to a pharmaceutical composition comprising the compound or fused heterocyclic derivative of general formula (I), or pharmaceutically acceptable salts thereof or prodrugs thereof. Finding a prodrug is an empirical exercise. Predicting, for example, if a certain compound is in fact a prodrug that produces the active compound metabolically at a therapeutic concentration and a useful rate, is filled with experimental uncertainty. Attempts have been made to predict drug metabolism de novo, but this is still an experimental science. A prodrug of a compound must meet three tests. It must itself be biologically active. It must be metabolized to a second substance in vivo at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be biologically active.

Determining whether a particular compound meets these three criteria requires a clinical trial setting and a large quantity of experimentation.

The State of the Prior Art

"Pro-drugs" are commonly known in the art as drugs which are administered in an inactive (or less active) form, and then metabolized in vivo into an active metabolite. As disclosed in Stella (Expert Opinions "Prodrugs as therapeutics"), "prodrugs are bioreversible derivatives of drug molecules used to overcome some barriers to the utility of the parent drug molecule. These barriers include, but are not limited to, solubility, permeability, stability, presystemic metabolism, and targeting limitations" (277). Stella, Valentino J, Expert Opinion of Therapeutic Patents, "Prodrugs as therapeutics," 2004 14(3): 277-280. Wolff et al. (Burger's Medicinal Chemistry, 5th Ed., Vol. 1, pgs. 975-977, 1994) summarizes the state of the prodrug art, the lengthy research involved in successfully identifying a prodrug, and difficulties of extrapolating between species. With the limited direction and exemplification the specification offers, it is highly unpredictable whether or not the compounds of the formula (I) will actually form effective prodrugs. Testa, Bernard, Biochemical Pharmacology, Prodrug Research: futile or fertile? 68 (2004) 2097-2106, discloses, on page 2098, the various challenges in prodrug research, concluding that all of these challenges may render prodrug optimization difficult to predict and achieve. Finally, Ettmayer, Peter, Medicinal Chemistry, Lessons Learned from Marketed and Investigational Prodrugs, 47(10) (2004) 2394-2404, discloses, on page 2401, that "the prodrug strategy should only be considered as a last resort to improve the oral bioavailability of important therapeutic agents" and "At the beginning of each prodrug program, there should be a clear definition of the problem to solve and defect to improve. The prodrug

approach should not be misunderstood as a universal solution to all barriers to a drug's usefulness, and on page 2402, "The majority of all prodrug approaches face the challenge of identifying the optimal prodrug plus its activation system to enhance or prolong the concentration of the active principle at the site of action. Because of the complex situation of prodrug transport and processing, we recommend, especially for novel prodrug principles, that the first step should be to design and investigate different prodrug prototypes of high diversity (different attachment sites, linkers, promoieties, hydrolytic, oxidative, reductive activation, chemical vs. enzymatic activation)." Ettmayer et al. concludes that "the focus on victorious prodrugs should not be misunderstood as neglecting the inherent difficulties and additional layers of complexity a prodrug strategy might face." The evidence supports the conclusion that the method of making claimed prodrugs is a subject for further study and experimentation.

The Level of Skill in the Art and the Predictability or lack thereof in the art

The level of skill of the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities as prodrugs. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any prodrug on its face, without evidence to support that particular prodrug. It is noted that the pharmaceutical art is unpredictable and requires the embodiments to be individually assessed for physiological activity. Thus, the more unpredictable the art, the more information in support of the invention is required to satisfy the statute. See In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970). Each embodiment of a

prodrug must be supported by this invention in order to be enabled for the full range of prodrugs of compounds of the Formula (9).

The Amount of Direction or Guidance Present

The specification discloses that "A prodrug of a compound represented by the above general formula (I) of the present invention can be prepared by introducing an appropriate group forming a prodrug into any one or more groups selected from a hydroxy group, an amino group, and a cyclic amino group such as a pyrazole ring, a piperazine ring or the like of the compound represented by the above general formula (I) using a corresponding reagent to produce a prodrug such as a halide compound or the like in the usual way, and then by suitably isolating and purificating in the usual way as occasion demands" (see page 71). However, as discussed above, it would be necessary for Applicant to provide evidentiary support for each embodiment due to the unpredictability in the art with regards to the success of prodrugs with some drugs over others. There are no working examples in the specification that show how to make or use prodrugs of the instantly claimed compounds. Additionally, the lack of examples in the specification is not sufficient to enable one skilled in the art to which it pertains to make and use any pharmaceutically acceptable prodrug as interpreted broadly by one of ordinary skill in the art. The specification does not adequately enable a method of making all prodrugs of the compounds that the claims encompass, as defined in the instant specification. The specification has limited exemplification thereof and of the necessary starting materials, as discussed supra.

As stated in Morton International Inc. v. Cardinal Chem, Co., 28 USPQ2d 1190: [T]he specification purports to each, with over fifty examples, the preparation of the claimed

compounds with the required connectivity. However... there is no evidence that such compounds exist... the examples of the patent do not produce the postulated compounds..., there is...no evidence that such compounds even exist.

The same circumstance is true here.

The Breadth of the Claims

The claims are drawn to any compound which is converted to a therapeutically active compound of the general formula (I) after administration, and the term should be interpreted as broadly in the instant application as is generally understood in the art. As discussed above, this broad disclosure cannot possibly enable one skilled in the art to which it pertains to make and use any pharmaceutically acceptable prodrug due to the unpredictability in the art with regards to the success of prodrugs with some drugs over others.

The specification provides limited support, as noted above, for the large number of prodrugs encompassed by the claims. The quantity of experimentation needed to make and use all of the prodrugs encompassed by the claims would be an undue burden on one skilled in the chemical art, since the skilled artisan is given inadequate guidance for the reasons state above. Even with the undue burden of experimentation, there is no guarantee that one would obtain the desired prodrugs in view of the Wolff reference.

The Quantity of Experimentation Needed

Based on the unpredictable nature of the invention and the state of the prior art and the breadth of the claims, one of ordinary skill in the pertinent art would be burdened with undue

experimentation study to determine whether any pharmaceutically acceptable prodrug of compounds of the formula (I) would successfully act as prodrugs as they are known in the art. Therefore, in view of the Wands factors discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which prodrugs, if any, would produce desired activity with compounds of the formula (I) with no assurance of success. This rejection can be overcome by the deletion of the words "prodrug thereof" from the rejected claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8.30am-5pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael C. Henry
March 11, 2010.

/Shaojia Anna Jiang/
Supervisory Patent Examiner
Art Unit 1623